#26

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	§	
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Iris Pecker et al.	§	
	§	
Serial No.: 09/322,977	§	
	§	
Filed: June 1, 1999	§	Group Art Unit: 1644
	§	
For: HEPARANASE SPECIFIC MOLECULAR PROBES AND THEIR USE IN RESEARCH AND MEDICAL APPLICATIONS	§	
	§	Attorney Docket: 00/20450
Examiner: M. Dibrino	§	(Previously 910/21)

Commissioner of Patents and Trademarks
Washington, D.C. 20231

DECLARATION OF ISRAEL VLODAVSKY UNDER 37 CFR 1.132

I am presently employed as researcher in the Hadassah-Hebrew University Hospital (Department of Oncology, Jeruasalem 91120, Israel). I chair the Tumor Biology Research Unit of the Sharett Oncology Institute of the Hadassah Hospital. I am a full professor in the Faculty of Medicine of the Hebrew University School of Medicine. I received my Ph.D degree from the Weizmann Institute of Science (Rehovot, Israel) in 1975, worked as a post-doctoral fellow in UCLA and UCSF and was a visiting Professor at Harvard Medical School (Children's Hospital, Boston). In 1980 I established a Tumor Biology Research Laboratory at the Hadassah-University Hospital. My research focuses on basic and clinical aspects of tumor metastasis and angiogenesis, with emphasis on cell interaction with the extracellular matrix, heparin-binding growth factors and heparin/heparan sulfate-degrading enzymes. Since the beginning of my carrier, I have published 247 scientific articles in highly regarded journals and books, and

have presented my achievements at more than 90 international scientific conferences. I am a member of several international scientific societies and important local committees, and was awarded the 1997 prize for a distinguished Israeli scientist in medicine. For the last 20 years I have been engaged in the research of heparanase and heparan sulfate and have published over 70 papers in the field (see enclosed curriculum vitae). I am the head and scientific director of the group that was the first to report the cloning and recombinant expression of the heparanase gene.

I am a co-inventor of the subject matter claimed in the above-referenced U.S. patent application.

I have read the Examiner's Office Action dated November 7, 2000. I hereby declare the following:

Heparanase has a specific, well characterized and unique catalytic activity known for over 20 years. Over the years, heparanase was partially purified from a variety of mammalian sources. Heparanase is defined as a GAG hydrolase which cleaves heparin and heparan sulfate (both are sulfated) at the β1,4 linkage between glucuronic acid and glucosamin. Heparanase is an endolytic enzyme and the average product length it generates is 8-12 saccharides. The other known heparin/heparan sulfate degrading enzymes are β-glucuronidase, α-L iduronidase and α-N acetylglucosaminidase. These three enzymes are exolytic enzymes, each of which cleaves a specific linkage within the polysaccharide chain and generates disaccharides. These issues are further addressed below.

There are three sources of reports regarding false heparanase antibodies as follows:

An anti PAI-1 antibody, which is described in U.S. Pat. No. 5,362,641, was produced in an attempt to elicit anti-heparanase antibodies. This antibody was

elicited by a PAI-1 contamination in a purified sample of heparanase, as was observed by peptide analysis.

Identification of this antibody as an anti PAI-1 antibody is discussed in U.S. Patent No. 5,968,822 (Application No. 08/922,170, from which priority is claimed. Page 11, line 18 to page 12, line 2, recite in this respect that:

> Several years ago we prepared rabbit polyclonal antibodies directed against our partially purified preparation of human placenta heparanase. These antibodies, referred to in U.S. Pat. No. 5,362,641, were later found to be directed against plasminogen activator inhibitor type I (PAI-1) that was co-purified with the placental heparanase. These findings led to a modification of the original purification protocol to remove the PAI-1 contaminant.

Another false anti-heparanase antibody was generated against the chemokine CTAP III, a protein that was reported to possess heparanase-like activity. These antibodies were generated by the group of Prof. Ledbetter as described in Hoogewerf et al. J Biol Chem 17;270(7):3268-77, 1995) and were donated to other researchers as reported by Kosir et al. (J Surg Res. 67(1):98-105, 1997, page 99, materials and methods, right column, western blot).

CTAP III is a low molecular weight chemokine, which has no homology to heparanase from human placenta, SK-hepatoma, platelets (Hullet et. al. Nat. Med 5(7): 803-809, 1999) and SV40 transformed fibroblasts (Toyoshima and Nakajima J. Biol. Chem. 274(34):24153-24160, 1999) which were all purified and cloned recently and correspond to the amino acid sequence set forth in SEQ ID NO. 2 of U.S. Patent No. 5,968,822 (Application No. 08/922,170).

Because CTAPIII and heparanase, as defined by SEQ ID NO:2 of U.S. Patent No. 5,968,822 (Application No. 08/922,170), share no sequence homology, these antibodies are irrelevant. In addition, it was declared and it is now accepted

by the scientific community, as is recited below, that CTAPIII was erroneously though to be heparanase.

The third false anti-heparanase antibody was generated in the laboratory of Prof. Nicolson and was first reported by Jin et al. (Int J Cancer. 45(6):1088-95, 1990). This group isolated a 96 kDa mouse protein and used a peptide derived from the N-terminus of the partially purified protein to generate polyclonal as well as monoclonal antibodies. These antibodies detect a 96 kDa protein, which is obviously different from the placental heparanase referred to in the instant application and which was later isolated from other tissues as currently reported by several other groups. These antibodies were used by several research groups in collaboration with either one of the authors of the original paper (Marchetti et al. Cancer Res. 56(12):2856-63, 1996, Marchetti and Nicolson, Adv Enzyme Regul. 37:111-34, 1997, Mollinedo et al. Biochem J. 327(3):917-23, 1997). In 1994, Vouge et al. (Int. J. Cancer 56:286-294, 1994) pointed out the fact that the antibodies claimed to detect heparanase actually detect GR94/endoplasmin, a previously cloned and characterized murine heat shock protein. The sequence and the molecular weight were in perfect agreement with those reported for the 96 kDa murine heparanase isolated by Nicolson's group. Later on, the mis-identification of the heparanase enzyme and consequently the antibodies generated against it was admitted and accepted by the scientific community. The late papers (1996, 1997) still referring to these antibodies, as heparanase specific, are obscure. There is no doubt, however, that those antibodies do not recognize heparanase. Interestingly, Prof. Nicolson has abandoned heparanase research and does not take part in the major progress achieved during the recent years. Dr. Nakajima is a researcher at Novartis, a company that published recently the cloning of heparanase, with Nakajima as a last author (Toyoshima and Nakajima, J. Biol. Chem. 274(34):24153-24160, 1999). The published sequence is identical to SEQ ID

NO:2 of U.S. Patent No. 5,968,822 (Application No. 08/922,170) and the molecular weight of the purified protein is of 50 kDa.

These falls anti-heparanase antibodies are further addressed below.

The following provides a more detailed insight relating to the catalytic activity of heparanase, which activity is known for over 20 years and is unique over all other heparin or heparan sulfate degrading enzymes.

The enzymatic degradation of glycosaminoglycans is reviewed By Ernst et al. (Critical Reviews in Biochemistry and Molecular Biology , 30(5):387-444 (1995)). Ernst et al. describe the structure of various GAGs, the enzymatic degradation process thereof and the enzymes involved in such degradation. The common feature of GAGs structure is repeated disaccharide units consisting of a uronic acid and hexosamine. Various GAGs differ in the composition of the dunits and in type and level of modifications, such as C5-epimerization and N or O-sulfation. Sulfated GAGs include heparin, heparan sulfate condroitin sulfate, dermatan sulfate and keratan sulfate. Heparan sulfate and heparin are composed of repeated units of glucosamine and glucuronic/iduronic acid, which undergo modifications such as C5-epimerization, N-sulfation and O-sulfation. Heparin is characterized by a higher level of modifications than heparan sulfate.

GAGs can be depolymerized enzymatically either by eliminative cleavage with lyases (EC 4.2.2.-) or by hydrolytic cleavage with hydrolases (EC 3.2.1.-). Often, these enzymes are specific for residues in the polysaccharide chain with certain modifications. GAG degrading lyases are mainly of bacterial origin. In the eliminative cleavage, C5 hydrogen of uronic acid is abstracted, forming an unsaturated C4-5 bond, whereas in the hydrolytic mechanism a proton is donated to the glycosidic oxygen and creating an O5 oxonium ion followed by water addition which neutralizes the oxonium ion and saturates all carbons (Lindhart et al. 1986, Appl. Biochem. Biotech. 12:135-75). The lyases

can only cleave linkages on the non-reducing side of the of uronic acids, as the carboxylic group of uronic acid participates in the reaction. The hydrolyses, on the other hand, can be specific for either of the two bonds in the repeating disaccharides.

In pages 414 and 424 of the review, tables 8 and 14, Ernst et al. list the known GAG degrading enzymes. These tables describe substrate specificity, cleavage mechanism, cleavage linkage, product length and mode of action (endo/exolytic). Heparanase is defined as a GAG hydrolase which cleaves heparin and heparan sulfate at the β1,4 linkage between glucuronic acid and glucosamin. Heparanase is an endolytic enzyme and the average product length is 8-12 saccharides.

The other known heparin/heparan sulfate degrading enzymes are β-glucuronidase, α-L iduronidase and α-N acetylglucosaminidase which are exolytic enzymes, each one which cleaves a specific linkage within the polysaccharide chain and generates disaccharides.

In table 8 the authors list two heparanases; platelet heparanase and tumor heparanase, which share the same substrate and mechanism of action. These two were later on found to be identical at the molecular level as well (Freeman et al. Biochem J. (1999) 342, 361-268, Vlodavsky et al. Nat. Med. 5(7):793-802, 1999, Hullet et al. Nature Medicine 5(7):803-809, 1999).

Thus, heparanase, which is known for over 20 years, has a unique and well characterized endolytic activity, endo-β-D-glucouronidase, towards heparin and heparan sulfate.

The phrase heparanase (endo-β-D-glucouronidase) protein" and hence monoclonal antibodies recognizing same relate to a specific and well defined group of species.

I turn now to a detailed discussion of the references cited by the Examiner in the recent Official action and which are said to teach anti-heparanase antibodies.

U.S. Pat. No. 5,332,812 describes the use of a solid phase substrate for determination of heparanase activity. An alternative approach for immuno-quantitation of heparanase is proposed, using heparanase specific antibodies. Column 11, lines 22-44 of U.S. Pat. No. 5,332,812 recite:

> The assay measuring levels of a glycosaminoglycan endoglycosidase such as heparan sulfate endoglycosidase (heparanase) may also be performed in an immunoassay format using polyclonal and/or monoclonal antibodies raised to the endoglycosidase. Preferably, antibodies with relatively low cross-reactivity to other endoglycosidases, such as the platelet endoglycosidase described by Oldberg, et al. (1980) Biochem., V 19, pp 5755-5762, can be used. The antibodies may be used with a variety of immunoassay techniques to measure the endoglycosidase protein directly. The endoglycosidase may be measured by either a radioimmunoassay described by Berson and Yalow (1968) Clin. Chem, Acta., V 22, p 51 or an immunoradiometric (IRMA) assay described by Miles, et al. (1976) Anal. Biochem., V 61, pp 209-224 using .sup.125 I-labeled antigen or antibody. The endoglycosidase may also be measured by an enzyme immunoassay that uses either a competitive-binding assay or a "sandwich" assay analogous to an IRMA and using alkaline phosphatase, horse radish peroxidase, or any other enzyme coupled to an antibody or to the endoglycosidase as reviewed by Wisdom (1976) Clin. Chem., V 22, pp 1243-1255. (emphasis added)

The concept of immunoassay of proteins using specific antibodies recognizing same is well known in the art for a long time. However, no example of an anti-heparanase antibody is disclosed in U.S. Pat. No. 5,332,812. The authors define the preferable antibody as non cross-reactive with the platelet

endoglycosidase described by Oldberg et al. (Biochem. 19:5755-5762, 1980). Oldberg et al. fail to describe or use in their paper any heparanase antibodies. Thus, the source for anti-heparanase antibodies remains obscure.

As is evident from the background section of the instant application, the response filed herewith (see in particular the concluding remarks, and the arguments) and this declaration, the need for anti-heparanase antibodies is well recognized for many years and many unsuccessful attempts were made to obtain such antibodies. U.S. Pat. No. 5,332,812 clearly recognizes a particular need for anti-heparanase antibodies, however, recognizing a need does not qualify as anticipation. The need for anti-heparanase antibodies is indeed recognized by the art. However, this need was not fulfilled by the prior art, nor does U.S. Pat. No. 5,332,812 fulfills this need.

Thus, U.S. Pat. No. 5,332,812 fails to teach anti-heparanase antibodies.

Marchetti et al. briefly mention the use of antibody developed against heparanase. No description of an antibody source, preparation or characteristics is provided. No data is shown regarding such an antibody. The authors refer to a manuscript in preparation. I failed to find any later publications which provide this data. In a similar paper published by Marchetti and Nicolson (Adv Enzyme Regul. 37:111-34, 1997) the same "results" are briefly described with the remark "data not shown" (see, page 127, the paragraph just before the discussion). In a more recent paper which discusses heparanase regulation in human melanoma and where Marchetti is the last author, the results are based solely on activity measurements (Walch et al. Int. J. Cancer 82:112-120, 1999). Mollinedo et al. (Biochem J. 327(3):917-23, 1997) report localization of heparanase using the monoclonal antibody and refer on page 918 (materials and methods, antibodies) to Marchetti at al. (Cancer Res. 56:2856-2863, 1996). Mollinedo et al. show immunoblots where the heparanase antibody detects a 96 kDa protein (page 920, Figure 2).

It is my knowledge that this antibody was generated in the laboratory of Prof. Nicolson and was first reported by Jin et al. (Int J Cancer. 45(6):1088-95, 1990). This group isolated a 96 kDa mouse protein and used a peptide derived from the N-terminus of the partially purified protein to generate polyclonal as well as monoclonal antibodies. These antibodies detect a 96 kDa protein, which is obviously different from placental heparanase and which was later isolated from other tissues as currently reported by several groups. These antibodies were used by several research groups in collaboration with either one of the authors of the original paper (Marchetti et al. Cancer Res. 56(12):2856-63, 1996, Marchetti and Nicolson, Adv Enzyme Regul. 37:111-34, 1997, Mollinedo et al. Biochem J. 327(3):917-23, 1997). In 1994, Vouge et al. (Int. J. Cancer 56:286-294, 1994) pointed out the fact that the antibodies claimed to detect heparanase actually detect GR94/endoplasmin, a previously cloned and characterized murine heat shock protein. The sequence and the molecular weight were in perfect agreement with those reported for the 96 kDa murine heparanase isolated by Nicolson's group. Later on, the mis-identification of the heparanase enzyme and consequentlythe antibodies generated against it was admitted and accepted by the scientific community (see attached declaration). The late papers (1996, 1997) still referring to these antibodies, as heparanase specific, are obscure. There is no doubt in my mind and it is well accepted by the scientific community that those antibodies do not recognize heparanase. Interestingly, Prof. Nicolson has abandoned heparanase research and does not take part in the major progress achieved during the recent years. Dr. Nakajima is a researcher at Novartis, a company that published recently the cloning of heparanase, with Nakajima as a last author (Toyoshima and Nakajima, J. Biol. Chem. 274(34):24153-24160, 1999). The published sequence is identical to SEQ ID NO:2 listed in U.S. Patent No. 5,968,822 (Application No. 08/922,170) and the molecular weight of the purified protein is of 50 kDa.

Heparanase is a very attractive enzyme. Besides the scientific interest its biological function suggests a clear pharmaceutical potential. Several research groups as well as biotechnology companies invested immense effort in purification and in cloning attempts. Following the first clues, four groups have cloned and published the heparanase sequence, all by means of activity assays, including, as already noted, Nakajima which was among the generators of the antibodies raised against the 96 kDa murine protein. It is very unlikely that a group having heparanase specific antibodies will not take advantage of such a powerful tool in cloning the heparanase gene. The recently published four independent reports define heparanase unequivocally and with a perfect consensus as a 50 kDa protein in human as well as in mouse and rat (Freeman et al. Biochem J. 342(2):361-368, 1999). This enzyme is clearly unrelated to the 97 kDa murine protein.

Kosir et al. provided yet another source of confusion in the field of heparanase, which confusion has now been resolved. Kosir et al. disclose anti-CTAP III antibodies, CTAP III is a platelet derives chemokine to which heparanase activity was erroneously attributed in the past. No sequence homology is observed between CTAP III and heparanases derived from, for example, placenta and from hepatoma cells (SEQ ID NO:2 of U.S. Patent No. 5,968,822 (Application No. 08/922,170), Vlodavsky et al. Nat. Med. 5(7):793-802, 1999, Kosir et al. Biochem Biophys Res Commun. 261(1):183-7, 1999) and as was later reported, from platelets (Hullet et al. Nature Medicine 5(7):803-809, 1999) and from SV40 transformed fibroblasts (Toyoshima and Nakajima J. Biol. Chem. 274(34):24153-24160, 1999).

The antibody used by Kosir at al. (J Surg Res. 67(1):98-105, 1997) was donated thereto by Dr. Ledbetter. According to lines 15-16 of the "Western blot" section, production of these antibodies was described in Hoogewerf et al. (J. Biol.

Chem. 270(7): 3268-77, 1995). In this paper Hoogwerf et al., a research group from Upjohn Company, Kalamazoo, Michigan, describe the identification of CXC chemokines (the CTAPIII family) as heparan sulfate degrading enzymes. The antibodies described in the paper were raised against CTAPIII, which shares no sequence homology with the 50 kDa heparanase. Moreover, in a recent paper the same group from Pharmacia and Upjohn, Inc. retracted from their earlier statement regarding the heparanase activity of CTAPIII (Fairbank et al. J Biol Chem 274(42): 29587-29590, 1999) page 29590, right column, last paragraph of the discussion. They state that:

> Finally, an earlier report from this laboratory suggested that heparanase was a post-translationally modified form of a CXC chemokine, namely CTAPIII (7). We have not been able to confirm this observation, nor have others who have purified and characterized human heparanase

In this paragraph they refer to their previous paper, Hoogewerf et al. (J Biol Chem 1995 Feb 17;270(7):3268-77) as discussed above.

It is accepted today by the scientific community that CTAPIII is not a heparanase or a precursor thereof.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United states Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

January 6, 2001

Israel Vlodavsky

Prof. Israel Vlodavsky

CURRICULUM VITAE

Name:	Israel Vlodavsky
Date & Place of Birth:	August 31, 1944, Israel
Nationality:	Israeli
Martial Status:	Married, three children
Military Service:	Israel Defence Forces (1963-65)

Education:

1968	B.Sc. Biochemistry and Microbiology, Hebrew University of Jerusalem.
1970	M.Sc. Department of Biochemistry, Hebrew University of Jerusalem. Thesis: "Properties of Calcium Binding and Active Transport in Sarcoplasmic Reitculum" under the supervision of Prof. Zvi Selinger.
1975	Ph.D. Weizmann Institute of Science, Rehovot, Israel. Thesis: "Lectins as Probe for Changes in Membrane Dynamics in Malignant Cell Transformation" under the supervision of Prof. Leo Sachs.
1976-1977	Postdoctoral Research under the supervision of Prof. C.F. Fox, Molecular Biology Institute, University of California, Los Angeles.
1977-1978	Postdoctoral Research under the supervision of Prof. D. Gospodarowicz, Cancer Research Institute, University of California, San Francisco.

Professional Experience:

1978-1979	Associate Research Biochemist, Cancer Research Institute, University of California, San Francisco.
1979-1981	Lecturer, Dept. of Radiation & Clinical Oncology Hadassah University Hospital, Jerusalem, Israel.
1981-1984	Senior Lecturer in Experimental Oncology, Dept. of Oncology, The Hebrew University-Hadassah Medical School.
1984-1990	Associate Professor in Experimental Oncology, Dept. of Oncology, The Hebrew University-Hadassah Medical School.
1985-1986	Visiting Professor, Dept. Surgical Research, Harvard Medical School, Boston.
1990-present	Professor, Dept. of Oncology, Hadassah-Hebrew University.

Current Position: Head, Tumor Biology Research Unit, Hadassah-Hebrew University Hospital.

1997	Elkeles prize - 1997 Distinguished scientist in Medicine

Ph.D. Students: Bar-Ner, M; Fridman, R; Bashkin, P; Benezra, M; Levi, E; Miao Hau-Quan; Elkin, M., Even-Ram, S.
Zecharia, E., Goldshmidt, O., Yedovitzky, Y., Bitan, M., Kovalshuk, O.; Aviv, A.

Key words: Extracellular Matrix; Angiogenesis; Metastasis; Heparan sulfate; Heparanase; Heparin-binding growth factors, Tumor progression

Research Topics:

1. Mammalian heparanase: Involovement in tumor metastasis and angiogenesis.
2. Mammalian heparanase: Involvement in inflammation and autoimmunity.
3. Heparan sulfate proteoglycans, heparin-binding growth factors and heparin-mimicking compounds.
4. Control of cell proliferation and differentiation by the extracellular matrix.
5. Vascular endothelial and smooth muscle cells, neo-vascularization and restenosis.

Research Fellowships and grants:

1976	Research Training Fellowship, UICC
1976	U.S. Public Health Service; Fogarty International Center
1977	Chaim Weizmann Postdoctoral Fellowship, Feinberg Graduate School,
1980-1983	The Israel Academy of Sciences
1980-1982	The Israel Cancer Research Fund (ICRF)
1980-1982	Israel Cancer Association
1981-1984	U.S.A.-Israel Binational Science Foundation
1981-1984	National Cancer Institute, NIH (RO1-CA 30289)
1983-1985	NCRD-DKFZ Cooperation in Cancer Research
1984-1987	The Israel Academy of Sciences
1984-1989	Leukemia Society of America
1985-1988	National Cancer Institute, NIH (RO1-CA 30289)
1987-1990	Applied Research Supported by KabiVitrum AB, Stockholm
1987-1993	Applied Research Supported by ImClone Systems, New York
1987-1990	U.S.A. - Israel Binational Science Foundation
1988-1990	The Israel Cancer Research Fund (ICRF)
1988-1991	German-Israel Foundation for Scientific Research & Development (GIF)
1988-1992	Applied Research Supported by Rhone-Poulenc Rorer Co.,Philadelphia
1989-1992	National Cancer Institute, NIH (ROl-CA 30289)
1992-1993	Ministry of Health.
1993-1994	The Israel Cancer Research Fund (ICRF)
1992-1995	U.S.A. - Israel Binational Science Foundation
1993-1996	The Israel Science Foundation
1993-1995	Applied Research Supported by IBEX Technologies, Montreal Quebec
1994-1998	The Israel Science Foundation (Excellence Research Center)
1995-1997	Ministry of Health
1995-1998	Joint German-Israeli Research Projects (MOSA-BMBF)
1996-1999	German-Israel Foundation for Scientific Research & Development (GIF)
1995-1997	Joint Japan-Israeli Research Projects
1996-2000	Applied Research Supported by Collgard/IPC, Medica Israel
1997-2000	Applied Research Supported by InSight pharmaceuticals Ltd., Israel
1998-2001	The Israel Science Foundation
1998-2001	Association for International Cancer Research, UK
1998-2000	Middle East Cancer Consortium (MECC)
1999-2002	NCRD-DKFZ Cooperation in Cancer Research
1999-2000	Center for the Study of Emerging Diseases
1999-2001	Hadasit-Applied Research
2000-2003	U.S Army Breast Cancer Program
2000-2002	NIH Breast Cancer Program

LIST OF PUBLICATIONS

1. Vlodavsky, I., Pick, U., and Selinger, Z. Properties of the phosphoprotein intermediate formed by the calcium transport ATPase of sarcoplasmic reticulum. Israel J. Chem. 9:28, 1971.

2. Vlodavsky, I., Inbar, M. and Sachs, L. Temperature sensitive agglutinability of human erythrocytes by lectins. Biochim. Biophys. Acta 274:364-368, 1972.

3. Inbar, M., Vlodavsky, I. and Sachs, L. Availability of L-Fucose-like sites on the surface membrane of normal and transformed mammalian cells. Biochim. Biophys. Acta 205:703-705, 1972.

4. Vlodavsky, I., Inbar, M. and Sachs, L. Membrane changes and adenosine triphosphate content in normal and malignant transformed cells. Proc. Natl. Acad. Sci. USA 70:1780-1784, 1973.

5. Shiloach, J., Bauer, S., Vlodavsky, I. and Selinger, Z. Phospholipase C from Bacillus Cereus: Production, purification and properties. Biotechnol. Bioneg. 15:551-558, 1973.

6. Vlodavsky, I. and Sachs, L. Difference in the cellular cholesterol to phospholipid ratio in normal lymphocytes and lymphocytic leukemic cells. Nature 250:67-68, 1974.

7. Vlodavsky, I. and Sachs, L. Lectin receptors on the cell surface membrane and the kinetics of lectin-induced cell agglutination. Exptl. Cell Res. 93:111-119, 1975.

8. Vlodavsky, I. and Sachs, L. Restriction of receptor mobility and the agglutination of cells by Concanavalin A. Exptl Cell Res. 96:202-214, 1975.

9. Vlodavsky, I., Fibach, E. and Sachs, L. Control of normal differentiation of myeloid leukemic cells: Glucose utilization, cellular ATP and associated membrane changes in D+ and D- cells. J. Cell Physiol. 87:167-178, 1976.

10. Lotem, J., Vlodavsky, I. and Sachs, L. Regulation of cap formation by concanavalin A and the differentiation of myeloid leukemic cells. Exptl. Cell Res. 101:323-330, 1976.

11. Vlodavsky, I. and Sachs, L. Difference in the calcium regulation of concanavalin A agglutinability and surface microvilli in normal and transformed cells: Relationship to membrane-cytoskeleton interaction. Expt. Cell Res. 105:179-189, 1977.

12. Aharonov, A., Vlodavsky, I., Pruss, R.M., Fox, C.F. and Herschman, H.R. Epidermal growth factor induced membrane changes in 3T3 cells. J. Cell Physiol. 95:195-202, 1978.

13. Vlodavsky, I., Fielding, P.E., Fielding, C.J. and Gospodarowicz, D. Role of contact inhibition in the regulation of receptor mediated uptake of low density lipoprotein in cultured endothelial cells. Proc. Natl. Acad. Sci. USA 75:356-360, 1978.

14. Vlodavsky, I., Brown, D. and Gospodarowicz, D. A comparison of the binding of epidermal growth factor to granulosa and luteal cells in tissue culture. J. Biol. Chem. 253:3744-3750, 1978.

15. Fielding, P.E., Vlodavsky, I., Gospodarowicz, D. and Fielding, C.J. Effect of contact inhibition on the regulation of cholestrol metabolism in cultured vascular endothelial cells. J. Biol. Chem. 254:749-755, 1979.

16. Fielding, C.J., Vlodavsky, I., Fielding, P.E. and Gospodarowicz, D. Characteristics of chylomicron binding and lipic uptake by endothelial cells in culture. J. Biol. Chem. 254:8861-8868, 1979.

17. Vlodavsky, I., Johnson, L.K., Fielding, P. and Gospodarowicz, D. Inhibition of low density lipoprotein uptake in confluent endothelial cell monolayers correlates with a restricted surface receptor redistribution. J. Cell Physiol. 100:481-496, 1979.

18. Goldminz, D., Vlodavsky, I., Johnson, L.K. and Gospodarowicz, D. The role of fibronectin and cellular morphology in the regulation of the selective permeability barrier properties of the corneal endothelium. Expt. Eye Res. 29:331-351, 1979.

19. Vlodavsky, I., Johnson, L.K. and Gospodarowicz, D. Appearance in confluent vascular endothelial cell monolayers of a specific cell surface protein (CSP-60) not detected in actively growing endothelial cells or in cell types growing in multiple layers. Proc. Natl. Acad. Sci. USA 76:2306-2310 and 4704, 1979.

20. Vlodavsky, I. and Gospodarowicz, D. Structural and functional alterations in the surface of vascular endothelial cells associated with the formation of a confluent cell monolayer and with the withdrawal of fibroblast growth factor. J. Supramolecular structure, 12:73-114, 1979.

21. Gospodarowicz, D., Greenburg, G., Vlodavsky, I., Alvarado, J. and Johnson, L.K. The identification and localization of fibronectin in cultured corneal endothelial cells: Cell surface polarity and physiological implications Expt. Eye Res. 29:485-509, 1979.

22. Vlodavsky, I., Greenburg, G., Johnson, L.K. and Gospodarowicz, D. Vascular endothelial cells maintained in the absence of fibroblast growth factor undergo structural and functional alterations that are incompatible with their in vivo differentiated properties. J. Cell Biol. 83:468-486, 1979.

23. Johnson, L.K., Baxter, J.D., Vlodavsky, I. and Gospodarowicz, D. Epidermal growth factor and expression of specific genes. Effects on cultured rat pituitary cells dissociable from the mitogenic response. Proc. Natl. Acad. Sci. USA, 77:394-398, 1980.

24. Greenburg, G., Vlodavsky, I., J.M. Foidart and Gospodarowicz, D. Medium from endothelial cell cultures can restore the normal phenotypic expression of vascular endothelium maintained in vitro in the absence of fibroblast growth factor. J. Cell Physiol. 105:333-347, 1980.

25. Savion, N., Vlodavsky, I. and Gospodarowicz, D. The role of the degradation process in the mitogenic effect of epidermal growth factor. Proc. Natl. Acad. Sci. USA 77:1466-1470, 1980.

26. Gospodarowicz, D., Delgado, D. and Vlodavsky, I. Permissive effect of the extracellular matrix on cell proliferation in-vitro. Proc. Natl. Acad. Sci. USA 77:4094-4098, 1980.

27. Vlodavsky, I., Liu, G.M. and Gospodarowicz, D. Morphological appearance, growth behavior and migratory activity of human tumor cells maintained on extracellular matrix vs plastic. Cell 19:607-616, 1980.

28. Johnson, L.K., Vlodavsky, I., Baxter, J.D. and Gospodarowicz, D. Nuclear accumulation of epidermal growth factor in rat pituitary cells. Nature 287:340-343, 1980.

29. Gospodarowicz, D., Vlodavsky, I. and Savion, N. The extracellular matrix and the control of proliferation of vascular endothelial and vascular smooth muscle cells. J. Supramol. Struc. 13:339-372, 1980.

30. Gospodarowicz, D., Vlodavsky, I. and Savion, N. The role of fibroblast growth factor and the extracellular matrix ir the control of proliferation and differentiation of corneal endothelial cells. Vision Res. 21:87-103, 1981.

31. Savion, N., Vlodavsky, I. and Gospodarowicz, D. Nuclear accumulation of epidermal growth factor in cultured bovine corneal endothelial and granulosa cells. J. Biol. Chem. 256:1149-1154, 1981.

32. Tauber, J.P., Goldminz, D., Vlodavsky, I. and Gospodarowicz, D. The interactions of the high density lipoproteins with cultured vascular endothelial cells. Eur. J. Biochem. 119:317-325, 1981.

33. Vlodavsky, I. and Gospodarowicz, D. Respective involvement of laminin and fibronectin in the adhesion of human carcinoma and sarcoma cells. Nature 289:304-306, 1981.

34. Stampfer, M., Vlodavsky, I., Riggs, J. and Smith, H.S. Fibronectin production by human mammary cells. J. Natl. Cancer Inst. 67:253-261, 1981.

35. Savion, N., Vlodavsky, I., Greenburg, G. and Gospodarowicz, D. Synthesis and distribution of cytoskeletal elements in cultured endothelial cells as a function of cell density. J. Cell Physiol. 110:129-141, 1982.

36. Vlodavsky, I., Voss, R., Yarkoni, A. and Fuks, Z. Stimulation of human amniotic fluid cell proliferation and colony formation by cell plating on a naturally produced extracellular matrix. Prenatal Diag. 2:13-23, 1982.

37. Vlodavsky, I., Levi, A., Lax, I., Schlessinger, J. and Fuks, Z. Induction of cell attachment and morphological differentiation in a pheochromocytoma cell line and embryonal sensory cells by the extracellular matrix. Develop. Biol. 93:285-300, 1982.

38. Vlodavsky, I., Ariav, Y., Atzmon, R. and Fuks, Z. Tumor cell attachment to the vascular endothelium and subsequent degradation of the subendothelial extracellular matrix. Relationship to cell metastasis. Expt. Cell Res. 140:149-159, 1982.

39. Kaiser, N., Vlodavsky, I., Tur-Sinai, A., Fuks, Z. and Cerasi, E. Binding, internalization and degradation of insulin in vascular endothelial cells. Diabetes 31:1077-1083, 1982.

40. Weisel, J.M., Gamliel, H., Vlodavsky, I., Gay, F. and Ben-Bassat, H. Cell attachment, growth characteristics and surface morphology of human upper respiratory tract epithelium cultured on extracellular matrix. Eur. J. Clin. Invest. 13:57-63, 1982.

41. Vlodavsky, I., Eldor, A., Hy-Am, E., Atzmon, R. and Fuks, Z. Platelet interaction with the extracellular matrix produced by cultured endothelial cells: A model to study the thrombogenicity of isolated subendothelial basal lamina. Thrombosis Res. 28:179-191, 1982.

42. Eldor, A., Vlodavsky, I., Atzmon, R., Hy-Am, E. and Fuks, Z. Cultured endothelial cells increase their capacity to synthesize prostacyclin following the formation of a contact inhibited cell monolayer. J. Cell Physiol. 114:179-183, 1982.

43. Eldor, A., Vlodavsky, I., Hy-Am, E., Atzmon, R. and Fuks, Z. The effect of radiation on the production of prostacyclin (PGI_2) by cultured vascular endothelial cells. Prostaglandins 25:263-281, 1983.

44. Vlodavsky, I., Schirrmacher, V., Ariav, Y. and Fuks, Z. Lymphoma cell interaction with cultured vascular endothelial cells and with the subendothelial basal lamina: Attachment, invasion and morphological appearance. Invasion and Metastasis 3:81-97, 1983.

45. Vlodavsky, I., Fuks, Z., Bar-Ner, M., Ariav, Y. and Schirrmacher, V. Lymphoma cell mediated degradation of sulfated proteoglycans in the subendothelial extracellular matrix: Relationship to tumor cell metastasis. Cancer Res. 43:2704-2711, 1983.

46. Eldor, A., Polliack, A., Vlodavsky, I. and Levy, M. Effects of dipyrone on prostaglandin production by human platelets and cultured bovine aortic endothelial cells. Thrombos. Haemostas. 49:132-137, 1983.

47. Lubetski-Korn, I., Ovadia, H., Vlodavsky, I., Fuks, Z. and Abramsky, O. Enhanced growth and morphological differentiation of isolated adult rat oligodendrocytes in vitro: Use of a naturally produced extracellular matrix. Brain Research 267:151-155, 1983.

48. Kaiser, N., Vlodavsky, I., Tur-Sinai, A., Fuks, Z. and Cerasi, E. Insulin binding and degradation in vascular endothelial cells: Modulation by cell growth and culture organization. Endocrinology 113:228-234, 1983.

49. Biran, S., Horowitz, A.T., Fuks, Z. and Vlodavsky, I. High density lipoprotein and extracellular matrix promotes growth and plating efficiency of normal human mammary epithelial cells in serum free medium. Int. J. Cancer 31:552-566, 1983.

50. Spira, O., Vlodavsky, I., Ulmansky, R., Atzmon, R., Fuks, Z., Gordon, A. and Gross, J. TSH and GH secretion and cell morphology in hypothyroid pituitary cell cultures grown on a natural extracellular matrix. Acta Endocrinol. 104:279-286, 1983.

51. Savion, N., Fuks, Z. and Vlodavsky, I. T lymphocytes and macrophages interaction with cultured vascular endothelial cells: Attachment, invasion and subsequent degradation of the subendothelial extracellular matrix. J. Cell Physiol. 118:169-176, 1984.

52. Eldor, A., Fridman, R., Vlodavsky, I., Hy-Am, E., Fuks, Z. and Panet, A. Interferon enhances prostacyclin production by vascular endothelial cells. J. Clin. Invest. 73:251-257, 1984.

53. Naparstek, Y., Cohen, I.R., Fuks, Z. and Vlodavsky, I. Activated T lymphocytes produce a matrix-degrading heparan sulfate endoglycosidase. Nature 310:241-243, 1984.

54. Yahalom, J., Eldor, A., Fuks, Z. and Vlodavsky, I. Degradation of sulfated proteoglycans in the subendothelial extracellular matrix by human platelet heparitinase. J. Clin. Invest. 74:1842-1849, 1984.

55. Hochner-Zelniker, D., Ron, M., Eldor, A., Fuks, Z. and Vlodavsky, I. Growth characteristics and functional properties of human first trimester decidua cells cultured in serum free medium. Biology of Reproduction. 31:827-836, 1984.

56. Ovadia, H., Vlodavsky, I., Abramsky, O. and Weidenfeld, J. Binding of hormonal steroids to isolated oligodendroglia and astroglia grown in vitro upon a naturally produced extracellular matrix. Clin. Neuropharmacol 7:307-311, 1984.

57. Ovadia, H., Lubetzki-Korn, I., Brenner, T., Abramsky, O., Fridman, R. and Vlodavsky, I. Adult rat oligodendrocytes grown in vitro upon an extracellular matrix have the ability to proliferate. Brain Res. 322:93-100, 1984.

58. Kramer, M., Robinson, P., Vlodavsky, I., Barz, D., Fridberger, P., Fuks, Z. and Schirrmacher, V. Characterization of extracellular matrix degrading protease derived from a highly metastatic tumor cell line. Eur. J. Cancer Clin. Oncol. 21:307-316, 1985.

59. Fridman, R., Ovadia, H., Fuks, Z. and Vlodavsky, I. Differential structural requirements for the induction of cell attachment, proliferation and differentiation by the extracellular matrix. Expt. Cell Res. 157:181-194, 1985.

60. Einhorn, S., Vlodavsky, Eldor, A., Fuks, Z. and Panet, A. Production and characterization of interferon from endothelial cells. J. Cell Physiol. 122:200-204, 1985.

61. Bar-Ner, M., Kramer, M., Schirrmacher, V., Ishai-Michaeli, R., Fuks, Z. and Vlodavsky, I. Sequential degradation of heparan sulfate in the subendothelial extracellular matrix by highly metastatic lymphoma cells. Int. J. Cancer, 35:483-491, 1985.

62. Spira, O., Halabi, A., Vlodavsky, I., Atzmon, R., Gross, J. and Gordon, A. Serum reduces the TSH Content in rat pituitary cells in culture. Acta Endocrinol. 109, 485-491, 1985.

63. Eldor, A., Vlodavsky, I., Martinowicz, U., Fuks, Z. and Coller, B.S. Platelet interaction with subendothelial extracellular matrix: Platelet-fibrinogen interactions are essential for platelet aggregation but not for the matrix induced release reaction. Blood, 65:1477-1483, 1985.

64. Yahalom, J., Eldor, A., Biran, S., Fuks, Z. and Vlodavsky, I. Platelet-tumor cell interaction with the subendothelial extracellular matrix: Relationship to cancer metastasis. Radiotherapy and Oncology, 3:211-225, 1985.

65. Fridman, R., Alon, Y., Doljansky, R., Fuks, Z. and Vlodavsky, I. Cell interaction with the extracellular matrices produced by endothelial cells and fibroblasts. Expt. Cell Res. 158-462-476, 1985.

66. Heyns, A.P., Eldor, A., Vlodavsky, I., Kaiser, N., Fridman, R. and Panet, A. Interferon inhibits the effect of platelet-derived growth factor on the proliferation of bovine aortic and smooth muscle cells: The antiproliferative and mitogenic effects in cell cycle events are independent. Expt. Cell. Res. 161:297-306, 1985.

67. Levine, R.F., Eldor, A., Hy-Am, E., Gamliel, H., Fuks, Z. and Vlodavsky, I. Megakariocyte interaction with subendothelial extracellular matrix is associated with adhesion, platelet-like shape change and thromboxane A production. Blood. 66:570-576, 1985.

68. Matzner, Y., Bar-Ner, M., Yahalom, J., Ishay-Michaeli, R., Fuks, Z. and Vlodavsky, I. Degradation of heparan sulfate in the subendothelial basement membrane by a readily released heparanase from human neutrophils, J. Clin. Invest. 76:1306-1313, 1985.

69. Pode, D., Horowitz, A.T., Vlodavsky, I. and Biran, S. The mechanism of human bladder tumor implantation in an in vitro model. J. Urol. 136:482-485, 1986.

70. Bar-Ner, M., Mayer, M., Schirrmacher, V. and Vlodavsky, I. Involvement of both heparanase and plasminogen activator in lymphoma cell mediated degradation of heparan sulfate in the subendothelial extra-cellular matrix. J. Cell Physiol. 128:299-307, 1986.

71. Biran, S., Vlodavsky, I., Fuks, Z. Lijovetzky, G. and Horowitz, A.T. Growth of human mammary carcinoma cells from biopsy specimens in serum-free medium on extracellular matrix. Int. J. Cancer, 38:345-354, 1986.

72. Furman, A., Rotmensch, S., Dor, J., Venter, A., Mashiach, S., Vlodavsky, I. and Amsterdam, A. Culture of human granulosa cells from an in vitro fertilization program: Effects of extracellular matrix on morphology and cyclic adenosine 3'5' monophosphate production. Fertil. Steril. 46:514-517, 1986.

73. Eldor, A., Vlodavsky, I., Fuks, Z., Muller, T.H. Eisert, W.G. Different effects of aspirin, dipyridamole and UD-CG 115 on platelet activation in a model of vascular injury: Studies with extracellular matrix covered with endothelial cells. Thrombos. Heamostas. 56:333-339, 1986.

74. Caine, Y.G., Vlodavsky, I., Hersh, M., Polliack, A., Gurfel, D., Or R., Levine, R.F. and Eldor, A. Adhesion, spreading and fragmentation of human megakaryocytes exposed to subendothelial extracellular matrix. A scanning electron microscopy study. Scanning Electron Microscopy, III 1087-1094, 1986.

75. Fridman, R., Lider, O., Naparstek, Y., Fuks, Z. Vlodavsky, I. and Cohen, I.R. Soluble antigen induces T lymphocytes to secrete an endoglycosidase that degrades the heparan sulfate moiety of subendothelial extracellular matrix. J. Cell Physiol. 130:85-94, 1987.

76. Pode, D., Horowitz, A.T., Vlodavsky, I., Shapiro, A. and Biran, S. Prevention of human bladder tumor cell implantation in an in vitro assay. J. Urol. 137:777-781, 1987.

77. Vlodavsky, I., Fridman, R., Sullivan, R., Sasse, J. and Klagsbrun, M. Aortic endothelial cells synthesize basic fibroblast growth factor which remains cell associated and platelet-derived growth factor which is secreted. J. Cell Physiol. 131:402-408, 1987.

78. Vlodavsky, I., Folkman, J., Sullivan, R., Fridman, R., Ishai-Michaelli, R., Sasse, J. and Klagsbrun, M. Endothelial cell-derived basic fibroblast growth factor: Synthesis and deposition into subendothelial extracellular matrix. Proc. Natl. Acad. Sci. USA, 84:2292-2296, 1987.

79. Bar-Ner, M., Eldor, A., Wasserman, L., Matzner, Y. and Vlodavsky, I. Inhibition of heparanase mediated degradation of extracellular matrix heparan sulfate by modified and non-anticoagulant heparin species. Blood, 70:551-557, 1987.

80. Eldor, A., Vlodavsky, I., Riklis, E. and Fuks, Z. Recovery of prostacyclin production capacity of irradiated endothelial cells and the protective effect of vitamin C. Prostaglandins 34:241-255, 1987.

81. Eldor, A., Bar-Ner, M., Yahalom, Y., Fuks, Z. and Vlodavsky, I. Role of heparanase in platelet and tumor cell interactions with subendothelial ECM. Seminars in Thrombos. Hemostas. 13:475-488, 1987.

82. Folkman, J., Klagsbrun, M., Sasse, J., Wadzinski, M., Ingber, D. and Vlodavsky, I. A heparin-binding angiogenic protein - basic fibroblast growth factor - is stored within basement membrane. Am. J. Pathol. 130:393-400, 1988.

83. Spira, O., Atzmon, R., Bar-Shavit, R., Gross, J., Gordon, A. and Vlodavsky, I. Striated muscle fibers differentiate in primary cultures of adult anterior pituitary cells. Endocrinology, 122:3002-3004, 1988.

84. Matzner, Y., Cohn, M., Vlodavsky, I., Hy-Am, E., Razin, E., Fuks, Z., Buchanan, M.R., Hass, T.A. and Eldor, A. Generation of lipid neutrophil chemoattractant by irradiated bovine aortic endothelial cells. J. Immunol. 140:2681-2685, 1988.

85. Krausz, M.M., Hartzstark, Z., Shlomai, Z., Gross, D., Matzner, Y., Eldor, A., Vlodavsky, I. and Ben-Bassat, H. Decreased neutrophil thromboxane A_2 and endothelial PGI_2 production in the postoperative period: An in vitro assay for detection of neutrophil and plasma dysfunction. Annals of Surg. 208:78-84, 1988.

86. Yahalom, J., Fibach, E., Bar-Tana, R., Fuks, Z. and I. Vlodavsky. Differentiating human leukemia cells express endoglycosidase that degrades heparan sulfate in subendothelial extracellular matrix. Leukemia Res. 12:711-717, 1988.

87. Vlodavsky, I., Ishai-Michaeli, R., Bar-Ner, M., Fridman, R., Horowitz, A.T., Fuks, Z. and Biran, S. Involvement of heparanase in tumor metastasis and angiogenesis. Is. J. Med. 24:464-470, 1988.

88. Lider, O., Baharav, E., Mekori, Y., Miller, T., Naparstek, Y., Vlodavsky, I. and Cohen, I.R. Suppression of experimental autoimmune diseases and prolongation of allograft survival by treatment of animals with heparinoid inhibitors of T lymphocyte heparanase. J. Clin. Invest. 83:752-756, 1989.

89. Birkenfeld, A., Ezra, Y., Ron, N., Navot, D., Granovsky, S., Schenker, J.G., Levij, I.S. and Vlodavsky, I. Indication of selective growth of human endometrial epithelial cells on extracellular matrix. In vitro 24:1182-1192, 1988.

90. Bashkin, P., Klagsbrun, M., Doctrow, S., Svahn, C-M., Folkman, J. and Vlodavsky, I. Basic fibroblast growth factor binds to subendothelial extracellular matrix and is released by heparanase and heparin-like molecules. Biochemistry 28:1737-1743, 1989.

91. Eldor, A., Fuks, Z., Matzner, Y., Witte, L.D. and Vlodavsky, I. Perturbation of endothelial functions by ionizing irradiation: effects of prostaglandins, chemoattractants and mitogens. Seminars in Thrombos. Hemostas. 15:215-225, 1989.

92. Amsterdam, A., Rotmensch, S., Furman, A., Venter, E.A., and Vlodavsky, I. Synergistic effect of human chroionic gonadotropin and extracellular matrix on *in vitro* differentiation of human granulosa cells: Progesterone production and gap junction formation. Endocrinology 124:1956-2004, 1989.

93. Rogelj, S., Klagsbrun, M., Atzmon, R., Kurokawa, M., Haimovitz, A., Fuks, Z., and Vlodavsky, I. Basic fibroblast growth factor is an extracellular matrix component required for supporting the proliferation of vascular endothelial cells and the differentiation of PC12 cells. J. Cell Biol. 109:823-831, 1989.

94. Bar-Shavit, R., Eldor, A. and Vlodavsky, I. Binding of thrombin to subendothelial extracellular matrix: Protection and expression of functional properties. J. Clin. Invest. 84:1096-1104, 1989.

95. Witte, L., Fuks, Z., Haimovitz, A., Vlodavsky, I., Goodman, D.S., and Eldor, A. Effects of irradiation on the release of growth factors from cultured bovine, porcine and human endothelial cells. Cancer Res. 49:5066-5072, 1989.

96. Resnick-Roguel, N., Burstein, H., Hamburger, J., Panet, A., Eldor, A., Vlodavsky, I., Kotler, M. Cytocidal effect caused by the envelope glycoprotein of a newly isolated avian hemangioma inducing retrovirus. J. Virology 63:4325-4330, 1989.

97. Eldor, A., Stromberg, R.R., Vlodavsky, I., Hy-Am, E., Koslow, A.R., Friedman, L.I. and Levine, R.F. The interaction of isolated megakaryocytes with subendothelial extracellular matrix in a perfusion chamber: The effect of shear stress on adhesion, shape change, and fragmentation. Blood cells, 17:447-454, 1991.

98. Chajek-Shaul, T., Friedman, G., Bengtsson-Olivecrona, G., Vlodavsky, I., and Bar-Shavit, R. Interaction of lipoprotein lipase with subendothelial extracellular matrix. Biochim. Biophys. Acta 1042-168-175, 1990.

99. Bashkin, P., Razin, E., Eldor, A., and Vlodavsky, I. Degranulating mast cells secrete an endoglycosidase which degrades heparan sulfate in subendothelial extracellular matrix. Blood 75:2204-2212, 1990.

100. Lider, O., Mekori, Y.A., Vlodavsky, I., Naparstek, Y., Baharav, E. and Cohen, I.R. Inhibition of T-lymphocyte heparanase by low dose heparin leads to impaired T lymphocyte traffic and reduced cellular immune reactivity in mice. Eur. J. Immunol. 20:493-499, 1990.

101. Bar-Shavit, R., Benezra, M., Eldor, A., Hy-Am, E., Fenton, J.W., Wilner, G. and Vlodavsky, I. Thrombin immobilized to extracellular matrix is a mitogen for vascular smooth muscle cells: Non-enzymatic mode of action. Cell Reg. 1:453-463, 1990.

102. Peretz, T., Antebi, S.U., Beller, U., Horowitz, A.T., Fuks, Z., and Vlodavsky, I. Maintenance on extracellular matrix and expression of heparanase activity by human ovarian carcinoma cells from biopsy specimens. Int. J. Cancer. 45:1054-1060, 1990.

103. Vlodavsky, I., Korner, G., Ishai-Michaeli, R., Bashkin, P., Bar-Shavit, R., and Fuks, Z. Extracellular matrix-resident growth factors and enzymes: Possible involvement in tumor metastasis and angiogenesis. Cancer Met. Rev. 9:203-226, 1990.

104. Cardon-Cardo, C., Vlodavsky, I., Haimovitz-Friedman, A., Hicklin, D., and Fuks, Z. Expression of basic fibroblast growth factor in normal human tissues. Lab. Invest. 63:832-840, 1990.

105. Matzner, Y., Vlodavsky, I., Ishai-Michaeli, R. and Eldor, A. Selective inhibition of neutrophil activation by the subendothelial extracellular matrix: possible role in protection of the vessel wall during diapedesis. Expt. Cell Res. 189:233-240, 1990.

106. Resnick-Roguel, N., Eldor, A., Panet, A., Vlodavsky, I., and Kotler, M. The envelope glycoprotein of avian hemangioma retrovirus induces a throbogenic surface on human and bovine endothelial cells. J. Virol. 64:4029-4032, 1990.

107. Yedgar, S., Vlodavsky, I., Panet, A., Reisfeld, N., and Eldor, A. Interferon enhances phospholipase A_2 activity in bovine aortic endothelial cells. Eicosanoids, 3:225-229, 1990.

108. Ishai-Michaeli, R., Eldor, A., and Vlodavsky, I. Heparanase activity expressed by platelets, neutrophils and lymphoma cells releases active fibroblast growth factor from extracellular matrix. Cell Reg. 1:833-842, 1990.

109. Vlodavsky, I., Fuks, Z., Ishai-Michaeli, R., Bashkin, P., Levi, E., Bar-Shavit, R., and Klagsbrun, M. Extracellular matrix-resident basic fibroblast growth factor: Implication for the control of angiogenesis. J. Cell. Biochem. 45:167-176, 1991.

110. Laskov, R., Ishai-Michaeli, R., Yefe-Nof, E., and Vlodavsky, I. Production of heparanase by normal and transformed murine B-lymphocytes. Int. J. Cancer. 47:92-98, 1991.

111. Bar-Shavit, R., Sabbah, V., Lampugnani, M.G., Marchisio, P.C., Fenton, J.W., Vlodavsky, I., and Dejana, E. An Arg-Gly-Asp sequence within thrombin promotes endothelial cell adhesion. J. Cell Biol. 112:335-345, 1991.

112. Vlodavsky, I., Svahn, C-M., Mohsen, M., Ishai-Michaeli, R., Eldor, A., and Fuks, Z. Heparan sulfate degradation ir tumor cell invasion an neovascularization. TIGS, 3:82-90, 1991.

113. Haimovitz-Friedman, A., Vlodavsky, I., Witte, L., and Fuks, Z. Autocrine effects of FGF in the repair of radiation damage in endothelial cells. Cancer Res., 51:2552-2558, 1991.

114. Haimovitz-Friedman, A., Falcone, D.J., Eldor, A., Schirrmacher, V., Vlodavsky, I., and Fuks, Z. Activation of platelet heparitinase by tumor cell derived factors. Blood, 78:789-796, 1991.

115. Godder, K., Vlodavsky, I., Eldor, A., Weksler, B.B., Haimovitz, A., and Fuks, Z. Heparanase activity in cultured endothelial cells. J. Cell. Physiol. 148:274-280, 1991.

116. Vlodavsky, I., Bar-Shavit, R., Ishai-Michaeli, R., Bashkin, P., and Fuks, Z. Extracellular sequestration and release of fibroblast growth factor: a regulatory mechanism? TIBS 16:268-271, 1991.

117. Vettel, V., Bar-Shavit, R., Simon, M.M., Bruner, G., Vlodavsky, I., and Kramer, M.D. Coexpression coordinate secretion and synergistic activity of T-cell associated serine proteinase-1 (MTSP-1) and heparanase of activated T-cells. Eur J. Immunol. 21:2247-2251, 1991.

118. Ishai-Michaeli, R., Svahn, C-M., Chajek-Shaul, T., Korner, G. Ekre, H-P., and Vlodavsky, I. Importance of size and sulfation of heparin in release of basic fibroblast factor from the vascular endothelium and extracellular matrix. Biochemistry 31: 2080-2088, 1992.

119. Bar-Shavit, R., Benezra, M., Sabbah, V., and Vlodavsky, I. Thrombin as a multifunctional protein: Induction of cell adhesion and proliferation. Am. J. of Respiratory Cell and Mol. Biol. 6: 123-129, 1992.

120. Bashkin, P., Gitay-Goren, H., Neufeld, G., and Vlodavsky, I. Release of cell surface associated basic FGF by phosphatidylinositol specific phospholipase C. J. Cell. Physiol. 151: 126-137, 1992.

121. Shneider, A., Uretzky, G., Schwalb, H., Mathias, K., Vlodavsky, and Melmed, R.N. An improved method for endothelial cell seeding on GORE-TEX small caliber vascular grafts. J. Vascular Surg. 15: 649-656, 1992.

122. Gitay-Goren, H., Soker, S., Vlodavsky, I., and Neufeld, G. Cell surface associated heparin-like molecules are required for the binding of vascular endothelial growth factor (VEGF) to its cell surface receptors. J. Biol. Chem. 267: 6093-6098, 1992.

123. Fuks, Z., Vlodavsky, I., Andreeff, M., and Haimovitz-Friedman, A. Effects of extracellular matrix on the response of endothelial cells to radiation in vitro. Eur. J. Cancer, 28A: 725-731, 1992.

124. Benezra, M., Vlodavsky, I., and Bar-Shavit, R. Thrombin enhancement of tumor cell heparanase. Exp. Cell Res. 201: 208-215, 1992.

125. Matzner, Y., Vlodavsky, I., Bar-Ner, M., Ishai-Michaeli, R., and Tauber, . Subcellular localization of heparanase in human neutrophils. J. Leukocyte Biol. 51:519-524, 1992.

126. Vlodavsky, I., Eldor, A., Haimovitz-Friedman, A., Matzner, Y., Ishai-Michaeli, R., Levi, E., Bashkin, P., Lider, O., Naparstek, Y., Cohen, I.R. and Fuks, Z. Expression of heparanase by platelets and circulating cells of the immune system: Possible involvement in diapedesis and extravasation. Invasion & Metastasis, 12: 112-127, 1992.

127. Benezra, M., Bar-Shavit, R., Yayon, A., Ben-Sasson, S., and Vlodavsky,I. Reversal of bFGF autocrine cell transformation by aromatic anionic compounds. Cancer Res. 52: 5656-5662, 1992.

128. Eisenberg, S., Sehayek, E., Olivecrona, T., and Vlodavsky, I. Lipoprotein lipase enhances binding of lipoproteins to heparan sulfate on cell surfaces and extracellular matrix. J. Clin. Invest. 90: 2013-2021, 1992.

129. Vlodavsky, I., Ishai-Michaeli, R., Mohsen, M., Bar-Shavit, R., Catane, R., Ekre, H.-P.T. and Svahn, C.M. Modulation of neovascularization and metastasis by species of heparin. Advances Exp. Biol. 313: 317-327, 1992.

130. Ekre, H-P., Naparstek, Y., Lider, Y., Hyden, P., Hagermark, O., Nilsson, T., Vlodavsky, I., and Cohen, I. Anti-inflammatory effects of heparin and its derivatives: inhibition of complement and of lymphocyte migration. Advances Exp. Biol. 313: 329-340, 1992.

131. Herskowiz, R., Miron, S., Gilat, D., Aderka, D., Wallach, D., Cohen, I.R., Vlodavsky, I., and Lider, O. Resting $CD4^+$ lymphocytes and antigen presenting cells are triggered to release TNF in response to injured extracellular matrix or its intact bound proteins. Immunology, 78: 50-57, 1993.

132. Korner, G., Bar-Ner, M., Bjornsson, T., Kuo, B.S. and Vlodavsky, I. Active plasminogen activator is deposited intc subendothelial extracellular matrix. J. Cell. Physiol. 154: 456-465, 1993.

133. Benezra, M., Vlodavsky, I., Neufeld, G., and Bar-Shavit, R. Thrombin-induced release of active basic fibroblast growth factor-heparan sulfate complexes from subendothelial extracellular matrix. Blood, 81:3324-3332, 1993.

134. Benezra, M., Vlodavsky, I., and Bar-Shavit, R. Prothrombin is converted to thrombin by plasminogen activator residing in the subendothelial extracellular matrix. Sem. Throm. Hemos. 19: 405-410, 1993.

135. Bar-Shavit, R., Eskohjido, Y., Fenton, J.W., Esko, J.D., and Vlodavsky. Thrombin adhesive properties: Induction by plasmin and heparan sulfate. J. Cell. Biol. 123: 1279-1287, 1993.

136. Korner, G., Deutsch, V.R., Vlodavsky, I., and Eldor, A. Effect of ionizing irradiation on endothelial cell transglutaminase. FEBS Lett. 330: 41-45, 1993.

137. Schneider, A., Schwalb, H., Vlodavsky, I., and Uretzky, G. An improved method of endothelial seeding on small caliber prosthetic vascular grafts coated with natural extracellular matrix. Clinical Materials 13:51-55, 1993.

138. Vettel, U., Brunner, G., Bar-Shavit, R., Vlodavsky, I., Kramer, M.D. Charge-dependent binding of granzyme A (MTSP-1) to basement membranes. Eur. J. Immunol. 23:279-282, 1993.

139. Naparstek, E., Slavin, S., Weiss, L., Sidi, H., Vlodavsky, I., and Naparstek, Y. Low-dose heparin inhibits acute graft versus host disease in mice. Bone Marrow Transplant 12:185-189, 1993.

140. Katz, A., Fish, A.J., Pe'er, J., Frucht-Rery, J., Ron, N., and Vlodavsky, I. Corneal entactin/Nidogen (E/N): Synthesis by corneal endothelial cells and distribution in the human cornea Invest. Ophthal & Vis. Sci. 35: 495-502, 1994.

141. Aviezer, D., Levi, E., Safran, M., Svahn, C-M., Buddecke, E., Schmidt, A., David, G., Vlodavsky, I., and Yayon, A. Differential structural requirements of heparan sulfate proteoglycans that promote bFGF-receptor binding. J. Biol. Chem. 269: 114-121, 1994.

142. Haimovitz-Friedman, A., Balaban, N., McLoughlin, M., Ehleiter, D., Michaeli, J., Vlodavsky, I., and Fuks, Z. Protein kinase C mediates basic fibroblast growth factor Protection of endothelial cell against radiation-induced apoptosis. Cancer Res. 54: 2591-2597, 1994.

143. Benezra, M., Ben-Sasson, S.A., Regan, J., Chang, M., Bar-Shavit, R., and Vlodavsky, I. Antiproliferative activity towards vascular smooth muscle cells and receptor binding of heparin-mimicking anionic aromatic compounds. Arteriosclerosis & Throm. 14: 1992-1999, 1994.

144. Soker, S., Svahn, C., Cohen, T., Levi, B-Z., Vlodavsky, I., and Neufeld, G. The effects of size and sulfation of defined fragments of heparin on the interaction of vascular endothelial growth factor (VEGF) with VEGF receptors Biochem. Biophys Res. Comm. 203: 1339-1347, 1994.

145. Gilat, M., Hershkoviz, R., Cahalon, L., Miron., S., Mekori,Y., Vlodavsky, I., and Lider, O. Regulation of adhesion of $CD4^+$ T Lymphocytes to intact or heparinase treated subendothelial extracellular matrix by diffusible or anchored RANTES and MIP-1β. J. Immunol. 153: 4899-4906, 1994.

146. Miao H-Q., Esko, J.D., Fritz, T.A., Yayon, A., and Vlodavsky, I. Restoration of bFGF-receptor binding by heparan sulfate primed on β-D-xylosides. J. Cell. Biochem. 57: 173-184, 1995.

147. Katz, B-Z., Ishai-Michaeli, R., Zusman, T., Vlodavsky, I., and Witz, I.P. Lung colonization by and heparanase activity in *in vitro* transformed 3T3 cells rendered highly tumorigenic by an *in vivo* passage. Invasion & Metastasis, 14: 276-289, 1995.

148. Vlodavsky, I., Mohsen, M., Lider, O., Ishai-Michaeli, R., Ekre, H.-P., Svahn, C.M., Vigoda, M., and Peretz, T. Inhibition of tumor metastasis by heparanase inhibiting species of heparin. Invasion & Metastasis, 14: 290-302, 1995.

149. Miao H-Q., Ishai-Michaeli, R., Peretz, T., and Vlodavsky, I. Laminarin sulfate mimics the effects of heparin on smooth muscle cell proliferatin and basic fibroblast growth factor receptor binding and mitogenic activity. J. Cell. Physiol. 164: 482-490, 1995.

150. Sehayek, E., Olivecrona, T., Olivecrona, G.B., Vlodavsky, I., Levkovitz, H., Avner, R., and Eisenberg, S. Binding to heparan sulfate is a critical and obligatory initial step during catabolism of lipoprotein lipase by HepG2 and other cell cultures. Atherosclerosis, 114: 1-8, 1995.

151. Guvakova, M., Vlodavsky, I., Yakubov, J.T., and Stein C.A. Phosphorothioate oligodeoxynucleotides bind to basic fibroblast growth factor, inhibit its binding to cell surface receptors, and remove it from low affinity binding sites on extracellular matrix. J. Biol. Chem. 270: 2620-2627, 1995.

152. Menashi, S., Vlodavsky, I., Ishai-Michaeli, R., and Fridman, R. Identification of gelatinase A in the subendothelial extracellular matrix. FEBS Lett. 361: 61-64, 1995.

153. Gilat, D., Hershkoviz, R., Cahalon, L., Korner, G., Vlodavsky, I., and Lider O. Molecular behavior adapts to context: Heparanase Functions as an extracellular matrix degrading enzyme or as a T cell adhesion molecule depending on the local pH. J. Exp. Med. 181: 1929-1934, 1995.

154. Bitan, M., Mohsen, M., Lider, O., Ishai-Michaeli, R., Ekre, H.-P., Svahn, C.M., Vigoda, M., Miao, H.Q., Levi, E., and Vlodavsky, I., and Peretz, T. Structural requierments for inhibition of melanoma cell metastasis by heparanase inhibiting species of heparin. Is. J. Med. 31: 106-118, 1995.

155. Vlodavsky, I., Miao H-Q., Atzmon, R., Levi, E., Zimmermann, J., Bar-Shavit, R. Peretz, T. and Ben-Sasson, S.A. Control of cell proliferation by heparan sulfate and heparin-binding growth factors. Thromb. Hemos. 74: 534-540, 1995

156. Bar-Shavit, R., Ginzburg,Y., Maoz, M., Vlodavsky, I., and Peretz, T. The involvement of thrombin RGD in metastasis: Characterization of a cryptic adhesive site. Is. J. Med. 31: 86-94, 1995.

157. Hershkovitz, R., Mor, F., Miao, H-Q., Vlodavsky, I., and Lider, O. Differential effects of polysulfated polysaccharide on experimental encephalomyelitis, proliferation of autoimmune T cells, and inhibition of heparanase activity. J. Autoimmunity. 8:
1955

158. Bar-Shavit, R., Maoz, M., Ginzburg,Y., and Vlodavsky, I. Specific involvement of glypican in thrombin adhesive properties. J. Cell Biochem. 61:278-291, 1996.

159. Miao H-Q., Ishai-Michaeli, R., Atzmon, R., Peretz, T. and Vlodavsky, I. Sulfate moieties in the subendothelial extracellular matrix are involved in bFGF swquestration, dimerization and stimulation of cell proliferation. J. Biol. Chem. 271: 4879-4886, 1996.

160. Ozeri, V., Tovi, A., Burstein, I., Natanson-Yaron, S., Caparon, G. C., Yamada, K. M., Akiyama, S. K., Vlodavsky, I., and Hanski, E. A novel two domain mechanism for streptococal adhesion to fibronectin. EMBO J. 15: 989-998 1996.

161. Levi, E., Miao, H.Q., Fridman, R., Yayon, A., and Vlodavsky, I. Matrix metalloproteinase-2 (MMP-2) releases active soluble ectodomain of fibroblast growth factor receptor-1. Proc. Natl. Acad. Sci. USA, 96: 7069-7074, 1996.

162. Vlodavsky, I., Miao, H.Q., Medalion, B., Danagher, P., and Ron, D. Involvement of heparan sulfate and related molecules in sequestration and growth promoting activity of fibroblast growth factor. Cancer Met. Rev. 15: 177-186, 1996.

163. Goshen, R., Hochberg, A., Korner, G., Levi, E., Ishai- Michaeli, R., Elkin, M., de Grot, N., and Vlodavsky, I. Purifi and characterization of placental heparanase and its expression by cultured cytotrophoblasts. Mol. Human Reprod. 2: 679-684, 1996.

164. Goshen, R., Ariel, I., Shuster, S., Hochberg, A., Vlodavsky, I., de Grot, N., Ben-Rafael , Z., and Stern, R. Hyaluronan, CD44 and its variant exons in human trophoblast invasion and placental angiogenesis. Mol. Human Rep 685-691, 1996.

165. Aharoni, D., Meiri, I., Atzmon, R., Vlodavsky, I., and Amsterdam, A. Differntial effect of components of the extracellular matrix on differentiation and programmed cell death. Current Biol. 7: 43-51,1996.

166. Sehayek, E., Wang, XX., Vlodavsky, I., Avner, R., Levkovitz, H., Olivecrona, T., Olivecrona, G., Willnow, T.E., Hertz, J., and Eisenberg, S. Heparan sulfate dependent and low density lipoprotein receptor related protein dependent catabolic pathway for lipoprotein lipase in mouse embryonic fibroblasts. Isr. J. Med. Sci. 32: 449-454, 19

167. Pines, M., Vlodavsky, I., and Nagler, A. Halofuginone hydrobromide. Drugs of the Futures, 21: 596-599, 1996.

168. Medalion, B., Merin, G., Aingorn, H., Miao, H-Q; Nagler, A; Elami, A; Ishai-Michaeli, R., and Vlodavsky, I. Endogenous basic fibroblast growth factor displaced by heparin from the luminal surface of human blood vess is preferentially sequestered by injured regions of the vessel wall". Circulation, 95: 1853-1862, 1997.

169. Nagler, A., Miao, H-Q, Eingorn, H., Slavin, S., Pines, M., and Vlodavsky, I. Inhibition of collagen synthesis, smooth muscle cell proliferation, and injury induced hyperplasia by halofuginone, Arteriosclerosis, Thrombosis & Vascular Biol. 17: 194-202, 1997.

170. Miao, H-Q., Ornitz, D. M., Eingorn, E., Ben-Sasson, S. A., and Vlodavsky I. Modulation of fibroblast growth factor-2 receptor binding, dimerization, signaling, and angiogenic activity by a synthetic heparin-mimicking polyanionic compound. J. Clin. Invest. 99: 1565-1575, 1997.

171. Bonneh-Barkay, D., Shlissel, M., Berman, B. Admon, A., Vlodavsky, I., Carey, D.J., Asundi, V.K. and Ron, D. Identification of glypican as a modulator of fibroblast growth factor-receptor interaction and biological activity. J. Biol. Chem. 272: 12415-12422, 1997.

172. Poltorak, Z., Cohen, T., Sivan, R., Spira, G., Vlodavsky, I., Keshet, E. and Neufeld, G. $VEGF_{145}$: a novel secreted VEGF form that binds to extracellular matrix. J. Biol. Chem. 272: 7151-7158, 1997.

173. Katz, A., Vlodavsky, I., Davies, M., Miao, H-Q., Ben-Sasson, S. A., Darmon, D., Hurwitz, H., Borgel, H M. Benezra, M. Antiproliferative activity to glomerular mesangial cells and receptor binding of heparin-mimicking polyaromatic anionic compound. J. Am. Soc. Nep. 8: 1688-1697, 1997.

174. Schneider, A., Chandra, M., Lazarovici, G., Vlodavsky, I., Merin, Uretzky, J. B., Borman, J. B., Schwalb, H Naturally produced extracellular matrix is an excellent substrate for canine endothelial cell proliferation an resistance to shear stress on PTFE vascular grafts. Thromb. Haemost. 78: 1392-1398, 1997.

175. Nagler, A., Katz, A., Aingorn, H., Miao, H-Q., Condiotti, R., Genina, O., Pines, M., and Vlodavsky, I. Inhibition of glomerular mesangial cell proliferation and extracellular matrix deposition by halofuginone, an inhibitor of collagen type I synthesis. Kidney Int. 52: 1561-1569, 1997.

176. Sandback-Pikas, D., Li, J-P., Vlodavsky, I., and Lindahl, U. Substrate specificity of heparanases from human hepatoma and platelets. J. Biol. Chem. 273: 18770-18777, 1998.

177. Even-Ram, S., Uzieli, B., Cohen, P., Granovsky, S., Maoz, M., Ginzburg, Y., Riech, R., Vlodavsky, I., and Bar-Shavit, R. Thrombin receptor overexpression in malignant and physiological invasion processes. Nature Med. 8: 909-914, 1998.

178. Hosokawa, K., Aharoni, D., Dantes, A., Shaulian, F., Atzmon, R., Kotsuji, F., Oren, M, Vlodavsky, I., and Amsterdam, A. Modulation of MDM2 expression and p53-induced apoptosis in immortalized human ovarian granulosa cells. Endocrinology, 139: 4688- 4700, 1998.

179. Hosokawa, K., Dantes, A., Schere-Levy, C., Barash, A., Kotsuji, F., Vlodavsky, I., and Amsterdam, A. Imduction of Ad4BP/SF-1, StAR and cytocrome P450scc enzyme system in newly established human granulosa cell lines. Endocrinology, 139: 4679-4687, 1998.

180. Rechter, M., Lider, O., Cahalon, L., Baharav, E., Dekel, M., Seigal, D., Vlodavsky, I., Aingorn, H., Cohen, I. R., an Shoseyov, O. A cellulose domain-fused recombinant human Tcell connective tissue-activating peptide-III manifests heparanase activity. Biochem. Biophys. Res. Comm. 255: 657-662, 1999.

181. Vlodavsky, I., Friedmann, Y., Elkin, M., Aingorn, H., Atzmon, A., Ishai-Michaeli, R., Bitan, M., Pappo, O., Peretz, Michal, I., Spector, L., and Pecker, I. Mammalian heparanase: gene cloning, expression and function in tumor progression and metastasis. Nature Medicine, 5: 793-802, 1999.

182. Elkin, M., Reich, R., Nagler, A., Aingorn, E., Pines, M., de-Groot, N., Hochberg, A., and Vlodavsky, I. Inhibition of matrix metalloproteinase-2 (MMP-2) expression and bladder carcinoma metastasis by halofuginone. Clinical Cancer Res., 5: 1982-1988, 1999.

183. Elkin, M., Ariel, I., Miao, H-Q., Nagler, A., Pines, M., de-Groot, N., Hochberg, A., and Vlodavsky, I. Inhibition of bladder carcinoma angiogenesis, stromal support and tumor growth by halofuginone. Cancer Res. 59: 4111-4118, 1999.

184. Schmidt, A., Vlodavsky, I., Volker, W., and Buddecke, E. Differentiation of coronary smooth muscle cells to a cell cycle arrested hypertrophic growth status by a synthetic non-toxic heparin-mimicking compound. Atherosclerosis, 147: 387-397, 1999

185. Miao, H-Q., Elkin, M., Aingorn, E., Ishai-Michaeli, R., Stein, C.A., and Vlodavsky, I. Inhibition of heparanase activ and tumor metastasis by laminarin sulfate and synthetic phosphorothioate oligodeoxynucleotides. Int. J. Cancer, 83: 424-431, 1999.

186. Berman, B., Ostrovsky, O., Shlissel, M., Lang, T., Regan, D., Vlodavsky, I., Ishai- Michaeli, R., and Ron. D. Similarities and differences between the effects of heparin and glypican-1 on the bioactivity of acidic fibroblast growth factor and keratinocyte growth factor. J. Biol. Chem. 274: 36132-36138, 1999.

187. Friedmann, Y., Vlodavsky, I., Aviv, A., Peretz, T., Pecker, I., and Pappo, O. Expression of heparanase in normal, dysplastic and neoplastic human colonic mucosa. Am. J. Pathol. 157: 1167-1175, 2000.

188. M. Elkin, H-Q. Miao, A. Nagler, E. Aingorn, R. Reich, I. Hemo, H-L. Dou, M. Pines and I. Vlodavsky. Halofuginone: a potent inhibitor of critical steps in angiogenesis progression. FASEB J. 14: 2477-2485.

189. A. Bentolila, I. Vlodavsky, R. Ishai-Michaeli, O. Kovalchuk, C. Haloun and A. J. Domb. Poly(n-acryl amino acids) - a new class of biologically active polyanions. J. Med. Chem. 43: 2591-2600, 2000.

190. Grisaru, D., Vlodavsky, I., Aingorn, H., Levavi, H., Eldor, A., Lessing, J.B., Pruss, D. and Friedmann, Y. Connectiv activating peptide III (CTAP-III) expression disappears in correlation with dysplasia in himan cervical epithelium. G Oncol. 79: 23-27, 2000.

191. Benezra, M., Vogel, T., Ben-Sasson, S., Panet , A., Sehayek, E., Eisenberg, S., and I. Vlodavsky. A synthetic heparin-mimicking polyanionic compound binds to the LDL receptor-related protein and inhibits vascular smooth cell proliferation. J. Cell. Biochem. In press.

192. Deutsch, V., Bitan, M., Friedmann, Y., Eldor, A., and Vlodavsky, I. Megakaryocyte maturation is associated with ex of the CXC chemokine connective tissue activating peptide III (CTAP-III). British J. Haematol. In press.

193. Neuger, L., Ruge, T., Makoveichuk, E., Vlodavsky, I., and Olivecrona, G. Effects of the heparin-mimicking compou RG-13577 on lipoprotein lipase and on lipase binding of LDL to cells. Atherosclerosis, In press.

194. Katz, A., Van-Dyk, D., Eingorn, E., Erman, A., Darmon, D., Horovitz, H., and Vlodavsky, I. Involvement of heparanase in the pathogenesis and early diagnosis of diabetic nephropathy. J. Am. Soc. Nep. Submitted.

195. Bar-Ami, S., Vlodavsky, I., Khoury, C., Seibel, M., Sommersberg, B., and Mayerhofer, A. A reduction of cumulus cell progesterone and estradiol-17β secretion by native extracellular matrix. Endocrinology, Submitted.

196. Schmidt, A., Vlodavsky, I., Volker, W., Sindermann, J. R., and Buddecke, E. Induction of a hypertrophic growth status of coronary smooth muscle cells is associated with overexpression of TGFβ. Submitted for publication. Submitted.

Book Chapters and Review Articles

1. Gospodarowicz, D., Vlodavsky, I., Fielding, P. and Birdwell, C.R. The effects of the epidermal and fibroblast growth factors upon cell proliferation using vascular and corneal endothelial cells as a model. In: Birth Defects (J.W. Littlefield and J. De Grouchy, Eds.) Exerpta Medica, Amsterdam, The Netherlands, pp 233-271, 1978.

2. Gospodarowicz, D., Vlodavsky, I., Bialecki, H. and Brown, K. The control of ovarian cell proliferation by the epidermal and fibroblast growth factors. In: Fifth Brook Lodge Meeting on Novel Aspects of Reproductive Biology (C.H. Spilman & J. Wilkes, eds) SP Medical and Scientific Books, Spectrum Pub. Inc., J. Wiley & Sons, New York, pp 107-178, 1978.

3. Gospodarowicz, D., Vlodavsky, I., Greenburg, G. and Johnson, L.K. Cellular shape is determined by the extracellular matrix and is responsible for the control of cellular growth and function. In: Hormones and Cell Culture (R. Ross and G. Sato, eds.) Cold Spring Harbor Conference on Cell Proliferation, V.6, Cold Spring Harbor, NY, 561-592, 1979.

4. Gospodarowicz, D., Vlodavsky, I., Greenburg, G., Alverado, J., Johnson, L.K. and Moran, J. Studies on atherogenesis and corneal transplantation using cultured vascular and corneal endothelia. Rec. Prog. in Hormone Res. 35:375-448, 1979.

5. Vlodavsky, I., and Gospodarowicz, D. Structural and functional alternations in the cell surface of vascular endothelial cells associated with the formation of a confluent monolayer and with the withdrawal of fibroblast growth factor. Prog. Clin. Biol. Res: Tumor Cell Surfaces and Malignancy (R.O. Hynes and C.E. Fox, eds) A.R. Liss Inc. New York, 41:439-481, 1980.

6. Gospodarowicz, D., Vlodavsky, I., Savion, N. and Johnson, L.K. The effect of EGF on cell proliferation and gene expression. In: Control Mechanisms in Animal Cells (L. Jiminez de Asua, R. Levi-Montalcini, R. Shields and S. Iacobelli, eds.) Raven Press, NY, pp 61-83, 1980.

7. Gospodarowicz, D., Vlodavsky, I., Savion, N. and Tauber, J. P. The control of proliferation and differentiation of vascular endothelial cells by fibroblast growth factor. In: Peptides: Integrators of Cell and Tissue Function, Society of General Physiologists Series, vol. 35 (F. Bloom, ed.) Raven Press, New York, pp 1-38, 1980.

8. Gospodarowicz, D., Vlodavsky, I., and Savion, N. The extracellular matrix and the control of proliferation of vascular endothelial and smooth muscle cells. Prog. Clin. Biol. Res: Control of cellular division and development (D. Cummingham, E. Goldwasser, J. Watson and C.F. Fox, eds.) A.R. Liss Inc., New York, 66:53-86, 1981.

9. Gospodarowicz, D., Vlodavsky, I., Greenburg, G. and Birdwell, C. The role of fibroblast and epidermal growth factors in the proliferative response of the vascular and corneal endothelium. In: The Growth Requirements of Vertebrate Cells *In vivo* (R.G. Ham, C. Waymouth and P.J. Chapple, eds.) Cambridge University Press, New York, pp 492-542, 1981.

10. Gospodarowicz, D. and Vlodavsky, I. The role of the extracellular matrix and growth factors in the control of proliferation of anchorage-dependent cells. In: Maturation factors in cnacer (M.A.S. Moore ed.) Prog. Cancer Res. Ther. Raven Press 22:73-104, 1982.

11. Gospodarowicz, D., Fujii, D.K., Giguere, L., Savion, N., Tauber, J.P. and Vlodavsky, I. The role of the basal lamina in cell attachment, proliferation and differentiation. Tumor cells vs normal cells. In: The Prostatic Cell: Structure and Function, Part A: Morphologic, Secretory and Biochemical Aspects (G.P. Murphy, A.A. Sandberg and J.P. Karr, eds.) Progress in Clinical and Biological Research 75A, A.R. Liss Inc., New York, pp 95-132, 1982.

12. Gospodarowicz, D., Fujii, D.K., and Vlodavsky, I. Basal lamina and the control of proliferation of malignant and normal cells. In: Expression of differentiated functions in cancer cells (R.P. Revoltella, G.M. Ponteri, C. Basilico, G. Rovera, R.C. Gallo and J.H. Subak-Sharpe, eds.) Raven Press, New York, pp 121-139, 1982.

13. Vlodavsky, I., Atzmon, R., Ariav, Y., and Fuks, Z. Control of cell shape, growth and differentiation by the extracellular matrix. In: Advances in Pathology (E. Levy, ed.) Pergamon Press, New York, 2:227-232, 1982.

14. Eldor, A., Vlodavsky, I., Hy-Am, E., Gamliel, H., Atzmon, R. and Fuks, Z. The thrombogenicity of the extracellula matrix produced by corneal endothelial cells in tissue culture. In: Advances in Pathology (E. Levy, ed.) Pergamon Press, New York, 1:413-416, 1982.

15. Schirrmacher, V., Waller, C. and Vlodavsky, I. In vitro invasion of lymphomas with different metastatic capacity. In: B and T cell tumors: Biological and clinical aspects, UCLA Symposia on Molecular and Cellular Biology. Vol XXIV (E. Vitetta and C.F. Fox, eds.) Academic Press, New York, pp 307-311, 1982.

16. Johnson, L.K., Vlodavsky, I. and Eberhardt, N.L. Nuclear actions of epidermal growth factor in rat pituitary tumor cells. In: Evolution of hormone-receptor systems, UCLA Symposia on Molecular and Cellular Biology (R.A. Bradshaw and G.N. Gill, eds) A.R. Liss Inc., New York V6 (New Series) pp 397-413, 1983.

17. Vlodavsky, I., Fuks, Z. and Schirrmacher, V. In vitro studies on tumor cell interaction with the vascular endothelium and subsequent degradation of the subendothelial extracellular matrix. In: The Endothelial Cell - A Pluripotent Control Cell of the Vessel Wall (D.G.S. Thilo and I. Freshney, eds.) S. Karger AG, Basel, pp 126-156, 1983.

18. Schirrmacher, V., and Vlodavsky, I. Interaction of metastatic and nonmetastatic tumor lines with aortic endothelial cell monolayer and their underlying basal lamina. In: Proc. 1st Eur. Conf. on Serum Free Cell Culture, Springer Verlag. pp 159-163, 1983.

19. Schirrmacher, V. and Vlodavsky, I. In vitro interactions of aortic endothelial cell monolayers with tumor cell lines of different invasive and metastatic capacity. In: Prog. appl. Microcirc. (K. Mebiner, ed.) S. Karger AG, Basel. Vol 1, pp 101-113, 1983.

20. Vlodavsky, I., Fuks, Z., Bar-Ner, M., Yahalom, J., Eldor, A., Savion, N., Naparstek, J., Cohen, I.R., Kramer, M. and Schirrmacher, V. Degradation of heparan sulfate in the subendothelial basement membrane by normal and malignant blood borne cells. In: Extracellular Matrix: Structure and Function, UCLA Symposia on Molecular and Cellular Biology (A.H. Reddi, ed.) 283-308, 1985.

21. Eldor, A., Levine, R.F., Caine, Y.G., Hy-Am, E. and Vlodavsky, I. Megakaryocyte interaction with the subendothelial extracellular matrix. In: Megakaryocyte development and function (Ed. Levine, R.F., Williams, N., Levin, J. and Evatt, B.L.) Alan R. Liss Inc. (N.Y.) Prog. Clin. Biol. Res. 215: 399-404, 1986.

22. Vlodavsky, I., Fuks, Z., Eisert, W.E. and Eldor, A. platelet interaction with subendothelial extracellular matrix: Effects of platelet inhibitor drugs. In: Radionuclide labeled cellular blood elements: Applications in atherosclerosis and thrombosis (Ed. A. du P. Heynes) pp 76-81, 1986.

23. Eldor, A., Hynes, A. du P., Vlodavsky, I. and Panet, A. Inhibitors of vascular smooth muscle proliferation: Effect o interferon and a prostacyclin analogue. In: Conference on Radionucleide labeled cellular blood elements: Applications in atherosclerosis and thrombosis (Ed. A. du P. Hynes) pp. 38-42, 1986.

24. Kramer, M.D., Schirrmacher, V. Bar-Ner, M. and Vlodavsky, I. A T-Lymphoma derived proteinase, sinergizing with an endoglycosidase in the degradation of sulphated proteoglycans in subendothelial extracellular matrix. In: Proteinases in inflammation and tumor invasion (Ed. H. Tschesche) Walter de Gruyter, Berlin. pp 373-393, 1986.

25. Eldor, A., Vlodavsky, I., du P. Heyns, A., Panet, A. The effect and interactions of interferon and arachidonate products with vessel wall cells. In: prostaglandins. Proceedings of the Third International Prostaglandin Symposium. Ed. H. Sinzinger, and K. Schror. Alan R. Liss Inc. (N.Y.) pp 323-328, 1987.

26. Vlodavsky, I., Klagsbrun, M. and Folkman, J. Storage of heparin binding endothelial cell growth factors in the cornea: A new mechanism for corneal neovascularization. In: Ocular Circulation and Neovascularisation (ed. Ben Ezra, D., Ryan, S.J., Glaser, B.M. and Murphy, R.P.) Nijhoff Publishers, Boston. pp 489-498, 1987.

63. Israel-France symposium on extracellular matrix (Jerusalem, April 1995)

64. Tumor microenvironment (Tiberias, May 1995)

65. XVth Int. Congress on Thrombosis & Haemostasis (Jerusalem, June 1995)

66. 6th Conference on Differentiation Therapy (Herzelia, June 1995)

67. The annual meeting of EVBA (Goteborg, Sweden, June 1996)

68. IX International Vascular Biology Meeting (Seattle, Washington, September 1996)

69. 4th Annual Scandinavian Atherosclerosis Conference (Copenhagen, May 1997)

70. 7th International Symposium on Cardiovascular Pharmacotherpy (Jerusalem 1997)

71. Denmark Symposium: Chronic Diseases Processes (Copenhagen, September 1997)

72. International Cancer Microenvironment Forum (London, October 1977)

73. Gordon Conference on proteoglycans (New Hampshire, July 1998)

74. Xth International Vascular Biology Meeting (Cairns, Australia, August 1998)

75. 70th European Atherosclerosis Society congress (Geneva, September, 1998)

76. F.I.S.E.B. (Israeli Societies of Experimental Biology-Eilat, December, 1998)

77. 1st Anglo-Israel Cancer Conference (Eilat, December, 1998).

78. Forbeck Focus Seminar on Tumor Metastasis (Ein-Cedi, February, 1999)

79. Wenner-Gren International Symposium (Stockholm, April, 1999)

80. The International Cancer Microenvironment Forum (Pittsburgh, October, 1999)

81. Vasculogenesis and Angiogenesis (Capri, October, 1999)

82. Bat-Sheva Seminar on Cell Adhesion (Dead Sea, November, 1999)

83. 91st. AACR annual meeting (San-Francisco, April, 2000)

84. Hinterzartener Kreis Cancer Progression meeting (Lake Como, Italy)

84. VIIIth Int. Congress, Metastasis Resaech Society (London, Sep. 2000)

85. 2nd. Int. Conference on Tumor Microenvironment (Tiberias, October, 2000)

86. AACR Conference on New Targets for Cancer Intervention (Eilat, Nov. 2000)

Teaching (courses taught)

- Biology of the cell (# 94625; structural and functional aspects; 1st year medical students).

- Growth factors and cytokines (# 81891, signaling and clinical applications).

- Selected topics in cancer research (# 94807; angiogenesis, metastasis).

- Cell-cell & Cell-matrix interactions (# 94843; Integrins, cell adhesion molecules, heparan sulfate proteoglycans and other components of the ECM).

- Other topics: Vascular Biology (vessel wall, restenosis, atherosclerosis).

University/Hospital activities

1986-1989	Head, Cell Biology Committee - Authority for Ph.D Research Students, The Hebrew University of Jerusalem.
1986-1990	Research Committee (Hadassah University Hospital).
1990-present	Board of Directors (Hadasit-Medical Research Services & Development Ltd.).
1991-present	Applied Research Committee (Hadassah University Hospital).
1995-present	Promotion Committee (Morphological & Biomedical Sciences; Faculty of Medicine, Hebrew University of Jerusalem).
1996-1999	Top Committee for Appointments & Promotions (Faculty of Medicine, Hebrew
1997-present	Steering Committee - Goldyne Savad Institute of Gene Therapy (Hadassah Medical Organization).

National & activities

1995 - 1998	Research grants Committee - Ministry of Health.
2000 - present	Head, Research grants Committee (Cell Biology) - The Israel Science Foundation.
2000 - present	Alon Committee - Council for Higher Education.
2000 - present	Science Vision Committee - Minister of Science, Culture & Education.